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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,302	09/26/2003	Hong Jin	7382-132-999	4464

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EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 12/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,302	JIN ET AL.	
	Examiner	Art Unit	
	Benjamin P. Blumel	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 27, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,13,18,19,21-46,53-55 and 58-60* is/are pending in the application.

4a) Of the above claim(s) *3, 13,21-44 and 58-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4, 5, 18, 19, 45, 46 and 53-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/2/04 and 4/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

Applicant's election of invention I in the reply filed on July 26, 2006 is acknowledged. However, applicants did not elect a species as directed in the Office Action of June 26, 2006. Therefore, on September 28, 2006 a communication we sent to the applicants addressing the requirement for an additional election of species with a response and proper election of species being received on October 27, 2006. Due to the election of position 176 containing a substituted amino acid as stated in claim 5 of the instant application, claims 3, 4, 13, 21-44 and 58-60 are withdrawn from consideration. Claims 1, 2, 4, 5, 18, 19, 45, 46, and 53-55 will be examined in the instant Office Action. Applicants are informed that prior art (Lu et al.) has been cited over the elected invention. However, since this rejection could be overcome without an amendment, a search of the species of claims 4 and 5 was expanded (position 172) and additional art has been cited (see Marriott et al. rejection below).

Information Disclosure Statement

The information disclosure statements (IDS) submitted on February 2, 2004 and April 16, 2004 were filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Objections

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the

reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification is objected to because the drawing description for figure 20 does not contain specific SEQ ID No:s for the presented nucleic acid sequences. In addition, the specification is also objected to because the amino acid sequences on pages 84 and 86-88, lines 14, 22; 12-15; 5, 12; and 5, 6, respectively do not contain specific SEQ ID NO:s.

Applicants must comply with sequence rules in order to be considered a complete response to this Office Action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4, 5, 18, 19, 45, 46 and 53-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 10, 11, 35, 39, 46, 48 and 53 of copending Application No. 10/811,508. Although the conflicting claims

are not identical, they are not patentably distinct from each other because the conflicting claims anticipate the elected invention of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 5, 18, 19, 45, 46 and 53-55 are rejected under 35 U.S.C. 102(a) as being anticipated by Lu et al., (Journal of Virology, 2002).

The instant invention is drawn to an immunologically effective amount of a live attenuated recombinant respiratory syncytial virus of subgroup A (RSV) with an attenuated phenotype and comprises a phosophoprotein (P) with one mutated or substituted amino acid residue. The altered amino acid residue is located at positions 172 or 176 of the P protein and this alteration eliminates a phosphorylation site. The instant invention is also drawn to the nucleic acid, which encodes the RSV of the instant invention.

Lu et al. teach the identification of an amino acid substitution within the phosophoprotein of RSV subgroup A. The use of recombinant RSV genomes with the substitution at positions

172 or 176 of the P protein resulted in an attenuated phenotype (decreased viral titer in lungs of mice and rats) and inhibited growth at 39°C. The attenuated RSV contained an amino acid substitution (Serine replaced Glycine) at position 172 or (Glycine replaced Glutamate) at position 176 of the P protein. This alteration resulted in the elimination of a phosphorylation site since Glutamate is one of the amino acids that can be phosphorylated, (see Table 1, Girault, Encyclopedia of Molecular Biology, 1999). However, the substitution at position 172 resulted in the addition of a phosphorylation site, which contradicts claims 18 and 19. In addition, the attenuated phenotype of the recombinant RSV could prove as an improved immunogen, which is ideal towards developing a vaccine for at risk groups (infants, toddlers, immunocompromised, etc.).

Claims 1, 2, 4, 5, 18, 19, 45, 46 and 53-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Marriott et al., (Journal of Virology, 1999).

The instant invention is drawn to an immunologically effective amount of a live attenuated recombinant respiratory syncytial virus of subgroup A (RSV) with an attenuated phenotype and comprises a phosophoprotein (P) with one mutated or substituted amino acid residue. The altered amino acid residue is located at positions 172 or 176 of the P protein. The instant invention is also drawn to the nucleic acid, which encodes the RSV of the instant invention.

Marriott et al. teach the identification of a temperature sensitive RSV of subgroup A, due to an amino acid substitution (Serine replaced Glycine) at position 172. Marriott et al. altered the amino acid position by introducing a point mutation into the nucleic acid of the RSV. The altered phenotype of the RSV utilized by Marriott et al. may prove to be useful towards the

development of an immunogenic composition. The amino acid substitution taught by Marriott et al. is the same residue change at position 172 of the instant application. However, this substitution adds a phosphorylation site, which contradicts what is stated in claims 18 and 19.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 18, 19 and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a RSV with an attenuated phenotype comprising an amino acid mutation at positions 172 and 176 of a phosphoprotein (P), does not reasonably provide enablement for all phosphoproteins with amino acid mutation(s). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The applicants have not enabled for a recombinant RSV of subgroup A having an attenuated phenotype, comprising a phosophoprotein (P) which comprises at least one amino acid substitution resulting in the lose of a phosphorylation site.

Nature of the invention. The claims are drawn to a recombinant RSV of subgroup A having an attenuated phenotype, comprising a phosophoprotein (P) which comprises at least one amino acid substitution resulting in the lose of a phosphorylation site.

State of the prior art. At the time the invention was made, the involvement of the phosphoprotein with regard to viral replication had been documented. For example, through a

series of deletions by Khattar et al., (Journal of General Virology, 2001), it had been determined that positions 161-180 and 221-241 were essential for P protein to interact with the N and L protein. In addition, Girault *supra* states 9 amino acids residues that can be phosphorylated there by changing some properties of proteins.

Breadth of the claims. The claims are very broad, covering any phosphoprotein with amino acid substitution(s), which resulted in an attenuated phenotype. The substitutions also result in a loss of a phosphorylation site, however, the substitution at position 172 resulted in the addition (Serine residue) of a phosphorylation site. The claims are not limited to a specific P protein from a specific organism, i.e. RSV or other virus.

Working examples. The effects of amino acid substitutions at positions 172 and 176 are analyzed for the effect on viral replication.

Guidance in the specification. The specification provides guidance towards introducing amino acid substitutions at various positions, however, only two substitutions stated in claims 4 and 5 were shown to result in an attenuated phenotype. Thus, the specification does not disclose the claimed recombinant RSV with amino acid substitutions of any P protein resulting in an attenuated phenotype.

Predictability of the art. At the time the invention was made, the involvement of the phosphoprotein with regard to viral replication had been documented. For example, through a series of deletions by Khattar et al. *supra*, it had been determined that positions 161-180 and 221-241 were essential for P protein to interact with the N and L protein.

Amount of experimentation necessary. Additional research is required in order to determine how effective amino acid substitutions of any phosphoprotein might be towards

attenuation of such a virus. Considering some experimentation has been completed based on the specification one might deduce that the same processes used in creating an attenuated RSV might reveal a working example. However, with out a representative number of phosphoproteins from different viruses (or at least a sequence comparison between viruses) with the amino acid substitution of the instant invention, one cannot expect to achieve the same phenotype as stated in the instant invention. Furthermore, the physical location of the amino acid substitution might have different effects on the P protein activity given the size and amino acid composition might differ between P proteins of various viruses. Applicants have generated an RSV of subgroup A with an attenuated phenotype through the substitution of an amino acid at positions 172 and 176, but the claim of any phosphoprotein with a similar substitution resulting in an attenuated phenotype of RSV has not been proven.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Summary

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin P. Blumel whose telephone number is 571-272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Benjamin Blumel
Patent Examiner

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice to Comply	Application No. 10/672,302	Applicant(s) Jin et al.	
	Examiner Benjamin Blumel	Art Unit 1648	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The disclosure is missing SEQ ID NO:s, see attached Action under Objections.

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
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